



PCT

## RAW SEQUENCE LISTING

DATE: 07/29/2004

PATENT APPLICATION: US/10/502,244

TIME: 16:11:53

Input Set : A:\seq\_1st\_US.txt

Output Set: N:\CRF4\07292004\J502244.raw

5 <110> APPLICANT: Carmeliet, Peter  
6 Moons, Lieve  
9 <120> TITLE OF INVENTION: A NOVEL TARGET TO INHIBIT ANGIOGENESIS  
13 <130> FILE REFERENCE: DECLE70.003APC  
C--> 16 <140> CURRENT APPLICATION NUMBER: US/10/502,244  
C--> 16 <141> CURRENT FILING DATE: 2004-07-22  
16 <150> PRIOR APPLICATION NUMBER: EP02075544.3  
18 <151> PRIOR FILING DATE: 2002-02-08  
22 <150> PRIOR APPLICATION NUMBER: EP02077742.1  
24 <151> PRIOR FILING DATE: 2002-07-09  
28 <150> PRIOR APPLICATION NUMBER: EP03100148.0  
30 <151> PRIOR FILING DATE: 2003-01-24  
34 <160> NUMBER OF SEQ ID NOS: 2  
38 <170> SOFTWARE: PatentIn version 3.1  
42 <210> SEQ ID NO: 1  
44 <211> LENGTH: 3794  
46 <212> TYPE: DNA  
48 <213> ORGANISM: Homo sapiens  
52 <220> FEATURE:  
54 <221> NAME/KEY: CDS  
56 <222> LOCATION: (38)..(2635)  
58 <223> OTHER INFORMATION:

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| 64 | Met Ala Leu Val Leu Gly  |     |
| 65 | 1 5  |     |
| 67 | tcc ctg ttg ctg ctg ggg ctg tgc ggg aac tcc ttt tca gga ggg cag  | 103 |
| 68 | Ser Leu Leu Leu Leu Gly Leu Cys Gly Asn Ser Phe Ser Gly Gly Gln  |     |
| 69 | 10 15 20   |     |
| 71 | cct tca tcc aca gat gct cct aag gct tgg aat tat gaa ttg cct gca  | 151 |
| 72 | Pro Ser Ser Thr Asp Ala Pro Lys Ala Trp Asn Tyr Glu Leu Pro Ala  |     |
| 73 | 25 30 35   |     |
| 75 | aca aat tat gag acc caa gac tcc cat aaa gct gga ccc att ggc att  | 199 |
| 76 | Thr Asn Tyr Glu Thr Gln Asp Ser His Lys Ala Gly Pro Ile Gly Ile  |     |
| 77 | 40 45 50   |     |
| 79 | ctc ttt gaa cta gtg cat atc ttt ctc tat gtg gta cag ccg cgt gat  | 247 |
| 80 | Leu Phe Glu Leu Val His Ile Phe Leu Tyr Val Val Gln Pro Arg Asp  |     |
| 81 | 55 60 65 70  |     |
| 83 | ttc cca gaa gat act ttg aga aaa ttc tta cag aag gca tat gaa tcc  | 295 |
| 84 | Phe Pro Glu Asp Thr Leu Arg Lys Phe Leu Gln Lys Ala Tyr Glu Ser  |     |
| 85 | 75 80 85   |     |
| 87 | aaa att gat tat gac aag cca gaa act gta atc tta ggt cta aag att  | 343 |
| 88 | Lys Ile Asp Tyr Asp Lys Pro Glu Thr Val Ile Leu Gly Leu Lys Ile  |     |

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| 91 gtc tac tat gaa gca ggg att att cta tgc tgt gtc ctg ggg ctg ctg  |     |     |     | 391  |
| 92 Val Tyr Tyr Glu Ala Gly Ile Ile Leu Cys Cys Val Leu Gly Leu Leu  |     |     |     |      |
| 93  | 105 | 110 | 115 |      |
| 95 ttt att att ctg atg cct ctg gtg ggg tat ttc ttt tgt atg tgt cgt  |     |     |     | 439  |
| 96 Phe Ile Ile Leu Met Pro Leu Val Gly Tyr Phe Phe Cys Met Cys Arg  |     |     |     |      |
| 97  | 120 | 125 | 130 |      |
| 99 tgc tgt aac aaa tgt ggt gga gaa atg cac cag cga cag aag gaa aat  |     |     |     | 487  |
| 100 Cys Cys Asn Lys Cys Gly Gly Glu Met His Gln Arg Gln Lys Glu Asn |     |     |     |      |
| 101 135   | 140 | 145 | 150 |      |
| 103 ggg ccc ttc ctg agg aaa tgc ttt gca atc tcc ctg ttg gtg att tgt |     |     |     | 535  |
| 104 Gly Pro Phe Leu Arg Lys Cys Phe Ala Ile Ser Leu Leu Val Ile Cys |     |     |     |      |
| 105   | 155 | 160 | 165 |      |
| 107 ata ata ata agc att ggc atc ttc tat ggt ttt gtg gca aat cac cag |     |     |     | 583  |
| 108 Ile Ile Ile Ser Ile Gly Ile Phe Tyr Gly Phe Val Ala Asn His Gln |     |     |     |      |
| 109   | 170 | 175 | 180 |      |
| 111 gta aga acc cgg atc aaa agg agt cgg aaa ctg gca gat agc aat ttc |     |     |     | 631  |
| 112 Val Arg Thr Arg Ile Lys Arg Ser Arg Lys Leu Ala Asp Ser Asn Phe |     |     |     |      |
| 113   | 185 | 190 | 195 |      |
| 115 aag gac ttg cga act ctc ttg aat gaa act cca gag caa atc aaa tat |     |     |     | 679  |
| 116 Lys Asp Leu Arg Thr Leu Asn Glu Thr Pro Glu Gln Ile Lys Tyr     |     |     |     |      |
| 117   | 200 | 205 | 210 |      |
| 119 ata ttg gcc cag tac aac act acc aag gac aag gcg ttc aca gat ctg |     |     |     | 727  |
| 120 Ile Leu Ala Gln Tyr Asn Thr Thr Lys Asp Lys Ala Phe Thr Asp Leu |     |     |     |      |
| 121 215   | 220 | 225 | 230 |      |
| 123 aac agt atc aat tca gtg cta gga ggc gga att ctt gac cga ctg aga |     |     |     | 775  |
| 124 Asn Ser Ile Asn Ser Val Leu Gly Gly Gly Ile Leu Asp Arg Leu Arg |     |     |     |      |
| 125   | 235 | 240 | 245 |      |
| 127 ccc aac atc atc cct gtt ctt gat gag att aag tcc atg gca aca gcg |     |     |     | 823  |
| 128 Pro Asn Ile Ile Pro Val Leu Asp Glu Ile Lys Ser Met Ala Thr Ala |     |     |     |      |
| 129   | 250 | 255 | 260 |      |
| 131 atc aag gag acc aaa gag gcg ttg gag aac atg aac agc acc ttg aag |     |     |     | 871  |
| 132 Ile Lys Glu Thr Lys Glu Ala Leu Glu Asn Met Asn Ser Thr Leu Lys |     |     |     |      |
| 133   | 265 | 270 | 275 |      |
| 135 agc ttg cac caa caa agt aca cag ctt agc agc agt ctg acc agc gtg |     |     |     | 919  |
| 136 Ser Leu His Gln Gln Ser Thr Gln Leu Ser Ser Ser Leu Thr Ser Val |     |     |     |      |
| 137   | 280 | 285 | 290 |      |
| 139 aaa act agc ctg cgg tca tct ctc aat gac cct ctg tgc ttg gtg cat |     |     |     | 967  |
| 140 Lys Thr Ser Leu Arg Ser Ser Leu Asn Asp Pro Leu Cys Leu Val His |     |     |     |      |
| 141 295   | 300 | 305 | 310 |      |
| 143 cca tca agt gaa acc tgc aac agc atc aga ttg tct cta agc cag ctg |     |     |     | 1015 |
| 144 Pro Ser Ser Glu Thr Cys Asn Ser Ile Arg Leu Ser Leu Ser Gln Leu |     |     |     |      |
| 145   | 315 | 320 | 325 |      |
| 147 aat agc aac cct gaa ctg agg cag ctt cca ccc gtg gat gca gaa ctt |     |     |     | 1063 |
| 148 Asn Ser Asn Pro Glu Leu Arg Gln Leu Pro Pro Val Asp Ala Glu Leu |     |     |     |      |
| 149   | 330 | 335 | 340 |      |
| 151 gac aac gtt aat aac gtt ctt agg aca gat ttg gat ggc ctg gtc caa |     |     |     | 1111 |
| 152 Asp Asn Val Asn Asn Val Leu Arg Thr Asp Leu Asp Gly Leu Val Gln |     |     |     |      |
| 153   | 345 | 350 | 355 |      |

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156 Gln Gly Tyr Gln Ser Leu Asn Asp Ile Pro Asp Arg Val Gln Arg Gln
157      360      365      370
159 acc acg act gtc gta gca ggt atc aaa agg gtc ttg aat tcc att ggt      1207
160 Thr Thr Thr Val Val Ala Gly Ile Lys Arg Val Leu Asn Ser Ile Gly
161 375      380      385      390
163 tca gat atc gac aat gta act cag cgt ctt cct att cag gat ata ctc      1255
164 Ser Asp Ile Asp Asn Val Thr Gln Arg Leu Pro Ile Gln Asp Ile Leu
165      395      400      405
167 tca gca ttc tct gtt tat gtt aat aac act gaa agt tac atc cac aga      1303
168 Ser Ala Phe Ser Val Tyr Val Asn Asn Thr Glu Ser Tyr Ile His Arg
169      410      415      420
171 aat tta cct aca ttg gaa gag tat gat tca tac tgg tgg ctg ggt ggc      1351
172 Asn Leu Pro Thr Leu Glu Glu Tyr Asp Ser Tyr Trp Trp Leu Gly Gly
173      425      430      435
175 ctg gtc atc tgc tct ctg ctg acc ctc atc gtg att ttt tac tac ctg      1399
176 Leu Val Ile Cys Ser Leu Leu Thr Leu Ile Val Ile Phe Tyr Tyr Leu
177      440      445      450
179 ggc tta ctg tgt ggc gtg tgc ggc tat gac agg cat gcc acc ccg acc      1447
180 Gly Leu Leu Cys Gly Val Cys Gly Tyr Asp Arg His Ala Thr Pro Thr
181 455      460      465      470
183 acc cga ggc tgt gtc tcc aac acc gga ggc gtc ttc ctc atg gtt gga      1495
184 Thr Arg Gly Cys Val Ser Asn Thr Gly Gly Val Phe Leu Met Val Gly
185      475      480      485
187 gtt gga tta agt ttc ctc ttt tgc tgg ata ttg atg atc att gtg gtt      1543
188 Val Gly Leu Ser Phe Leu Phe Cys Trp Ile Leu Met Ile Ile Val Val
189      490      495      500
191 ctt acc ttt gtc ttt ggt gca aat gtg gaa aaa ctg atc tgt gaa cct      1591
192 Leu Thr Phe Val Phe Gly Ala Asn Val Glu Lys Leu Ile Cys Glu Pro
193      505      510      515
195 tac acg agc aag gaa tta ttc cgg gtt ttg gat aca ccc tac tta cta      1639
196 Tyr Thr Ser Lys Glu Leu Phe Arg Val Leu Asp Thr Pro Tyr Leu Leu
197      520      525      530
199 aat gaa gac tgg gaa tac tat ctc tct ggg aag cta ttt aat aaa tca      1687
200 Asn Glu Asp Trp Glu Tyr Tyr Leu Ser Gly Lys Leu Phe Asn Lys Ser
201 535      540      545      550
203 aaa atg aag ctc act ttt gaa caa gtt tac agt gac tgc aaa aaa aat      1735
204 Lys Met Lys Leu Thr Phe Glu Gln Val Tyr Ser Asp Cys Lys Lys Asn
205      555      560      565
207 aga ggc act tac ggc act ctt cac ctg cag aac agc ttc aat atc agt      1783
208 Arg Gly Thr Tyr Gly Thr Leu His Leu Gln Asn Ser Phe Asn Ile Ser
209      570      575      580
211 gaa cat ctc aac att aat gag cat act gga agc ata agc agt gaa ttg      1831
212 Glu His Leu Asn Ile Asn Glu His Thr Gly Ser Ile Ser Ser Glu Leu
213      585      590      595
215 gaa agt ctg aag gta aat ctt aat atc ttt ctg ttg ggt gca gca gga      1879
216 Glu Ser Leu Lys Val Asn Leu Asn Ile Phe Leu Leu Gly Ala Ala Gly
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219 aga aaa aac ctt cag gat ttt gct gct tgt gga ata gac aga atg aat      1927

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| 220 | Arg        | Lys        | Asn         | Leu        | Gln        | Asp        | Phe | Ala | Ala | Cys | Gly | Ile | Asp        | Arg | Met | Asn |      |
| 221 | 615        |            |             |            |            | 620        |     |     |     |     | 625 |     |            |     |     | 630 |      |
| 223 | tat        | gac        | agc         | tac        | ttg        | gct        | cag | act | ggg | aaa | tcc | ccc | gca        | gga | gtg | aat | 1975 |
| 224 | Tyr        | Asp        | Ser         | Tyr        | Leu        | Ala        | Gln | Thr | Gly | Lys | Ser | Pro | Ala        | Gly | Val | Asn |      |
| 225 |            |            |             |            | 635        |            |     |     |     | 640 |     |     |            |     | 645 |     |      |
| 227 | ctt        | tta        | tca         | ttt        | gca        | tat        | gat | cta | gaa | gca | aaa | gca | aac        | agt | ttg | ccc | 2023 |
| 228 | Leu        | Leu        | Ser         | Phe        | Ala        | Tyr        | Asp | Leu | Glu | Ala | Lys | Ala | Asn        | Ser | Leu | Pro |      |
| 229 |            |            |             |            | 650        |            |     |     | 655 |     |     |     |            | 660 |     |     |      |
| 231 | cca        | gga        | aat         | ttg        | agg        | aac        | tcc | ctg | aaa | aga | gat | gca | caa        | act | att | aaa | 2071 |
| 232 | Pro        | Gly        | Asn         | Leu        | Arg        | Asn        | Ser | Leu | Lys | Arg | Asp | Ala | Gln        | Thr | Ile | Lys |      |
| 233 |            |            |             |            | 665        |            |     |     | 670 |     |     |     |            | 675 |     |     |      |
| 235 | aca        | att        | cac         | cag        | caa        | cga        | gtc | ctt | cct | ata | gaa | caa | tca        | ctg | agc | act | 2119 |
| 236 | Thr        | Ile        | His         | Gln        | Gln        | Arg        | Val | Leu | Pro | Ile | Glu | Gln | Ser        | Leu | Ser | Thr |      |
| 237 |            |            |             |            | 680        |            |     |     | 685 |     |     |     |            | 690 |     |     |      |
| 239 | cta        | tac        | caa         | agc        | gtc        | aag        | ata | ctt | caa | cgc | aca | ggg | aat        | gga | ttg | ttg | 2167 |
| 240 | Leu        | Tyr        | Gln         | Ser        | Val        | Lys        | Ile | Leu | Gln | Arg | Thr | Gly | Asn        | Gly | Leu | Leu |      |
| 241 | 695        |            |             |            |            | 700        |     |     |     |     | 705 |     |            |     | 710 |     |      |
| 243 | gag        | aga        | gta         | act        | agg        | att        | cta | gct | tct | ctg | gat | ttt | gct        | cag | aac | ttc | 2215 |
| 244 | Glu        | Arg        | Val         | Thr        | Arg        | Ile        | Leu | Ala | Ser | Leu | Asp | Phe | Ala        | Gln | Asn | Phe |      |
| 245 |            |            |             |            | 715        |            |     |     |     | 720 |     |     |            |     | 725 |     |      |
| 247 | atc        | aca        | aac         | aat        | act        | tcc        | tct | gtt | att | att | gag | gaa | act        | aag | aag | tat | 2263 |
| 248 | Ile        | Thr        | Asn         | Asn        | Thr        | Ser        | Ser | Val | Ile | Ile | Glu | Glu | Thr        | Lys | Lys | Tyr |      |
| 249 |            |            |             |            | 730        |            |     |     | 735 |     |     |     |            | 740 |     |     |      |
| 251 | ggg        | aga        | aca         | ata        | ata        | gga        | tat | ttt | gaa | cat | tat | ctg | cag        | tgg | atc | gag | 2311 |
| 252 | Gly        | Arg        | Thr         | Ile        | Ile        | Gly        | Tyr | Phe | Glu | His | Tyr | Leu | Gln        | Trp | Ile | Glu |      |
| 253 |            |            |             |            | 745        |            |     |     | 750 |     |     |     |            | 755 |     |     |      |
| 255 | ttc        | tct        | atc         | agt        | gag        | aaa        | gtg | gca | tgc | tgc | aaa | cct | gtg        | gcc | acc | gct | 2359 |
| 256 | Phe        | Ser        | Ile         | Ser        | Glu        | Lys        | Val | Ala | Ser | Cys | Lys | Pro | Val        | Ala | Thr | Ala |      |
| 257 |            |            |             |            | 760        |            |     |     | 765 |     |     |     |            | 770 |     |     |      |
| 259 | cta        | gat        | act         | gct        | gtt        | gat        | gtc | ttt | ctg | tgt | agc | tac | att        | atc | gac | ccc | 2407 |
| 260 | Leu        | Asp        | Thr         | Ala        | Val        | Asp        | Val | Phe | Leu | Cys | Ser | Tyr | Ile        | Ile | Asp | Pro |      |
| 261 | 775        |            |             |            |            | 780        |     |     |     |     | 785 |     |            |     | 790 |     |      |
| 263 | ttg        | aat        | ttg         | ttt        | tgg        | ttt        | ggc | ata | gga | aaa | gct | act | gta        | ttt | tta | ctt | 2455 |
| 264 | Leu        | Asn        | Leu         | Phe        | Trp        | Phe        | Gly | Ile | Gly | Lys | Ala | Thr | Val        | Phe | Leu | Leu |      |
| 265 |            |            |             |            | 795        |            |     |     | 800 |     |     |     |            |     | 805 |     |      |
| 267 | ccg        | gct        | cta         | att        | ttt        | gcg        | gta | aaa | ctg | gct | aag | tac | tat        | cgt | cga | atg | 2503 |
| 268 | Pro        | Ala        | Leu         | Ile        | Phe        | Ala        | Val | Lys | Leu | Ala | Lys | Tyr | Tyr        | Arg | Met |     |      |
| 269 |            |            |             |            | 810        |            |     |     | 815 |     |     |     |            | 820 |     |     |      |
| 271 | gat        | tgc        | gag         | gac        | gtg        | tac        | gat | gat | gtt | gaa | act | ata | ccc        | atg | aaa | aat | 2551 |
| 272 | Asp        | Ser        | Glu         | Asp        | Val        | Tyr        | Asp | Asp | Val | Glu | Thr | Ile | Pro        | Met | Lys | Asn |      |
| 273 |            |            |             |            | 825        |            |     |     | 830 |     |     |     |            | 835 |     |     |      |
| 275 | atg        | gaa        | aat         | ggg        | aat        | aat        | ggg | tat | cat | aaa | gat | cat | gta        | tat | ggg | att | 2599 |
| 276 | Met        | Glu        | Asn         | Gly        | Asn        | Asn        | Gly | Tyr | His | Lys | Asp | His | Val        | Tyr | Gly | Ile |      |
| 277 |            |            |             |            | 840        |            |     |     | 845 |     |     |     |            | 850 |     |     |      |
| 279 | cac        | aat        | cct         | gtt        | atg        | aca        | agc | cca | tca | caa | cat | tga | tagctgatgt |     |     |     | 2645 |
| 280 | His        | Asn        | Pro         | Val        | Met        | Thr        | Ser | Pro | Ser | Gln | His |     |            |     |     |     |      |
| 281 | 855        |            |             |            |            | 860        |     |     |     |     |     |     |            | 865 |     |     |      |
| 283 | tgaaactgct | tgagcatcag | gataactcaaa | gtggaaagga | tcacagattt | ttggtagttt |     |     |     |     |     |     |            |     |     |     | 2705 |
| 285 | ctgggtctac | aaggactttc | caaatccagg  | agcaacgcca | gtggcaacgt | agtgactcag |     |     |     |     |     |     |            |     |     |     | 2765 |

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287 gcgggcacca aggcaacggc accattggtc tctgggtagt gctttaagaa.tgaacacaat 2825
289 cacgttatag tccatgggcc atcactattc aaggatgact cccccccttc ctgtctatatt 2885
291 ttgtttttta cttttttaca ctgagtttct atttagacac tacaacatat ggggtgtttg 2945
293 ttcccattgg atgcatttct atcaaaactc tatcaaatgt gatggctaga ttctaacata 3005
295 ttgccatgtg tggagtgtgc tgaacacaca ccagtttaca ggaaagatgc attttgtgta 3065
297 cagtaaacgg tgtatatacc ttttgttacc acagagtttt ttaaacaaat gagtattata 3125
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315 acaaggtaaa tattcatttg cttcaggagt ttcattgttg atctgtcatt atcaaaagtg 3665
317 atcagcaatg aagaactggt cggacaaaat ttaacgttga tgtaatggaa ttccagatgt 3725
319 aggcattccc cccaggtctt ttcattgtgc gattgcagtt ctgattcatt tgaataaaaa 3785
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324 &lt;210&gt; SEQ ID NO: 2

326 &lt;211&gt; LENGTH: 865

328 &lt;212&gt; TYPE: PRT

330 &lt;213&gt; ORGANISM: Homo sapiens

334 &lt;400&gt; SEQUENCE: 2

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341 20 25 30
344 Asn Tyr Glu Leu Pro Ala Thr Asn Tyr Glu Thr Gln Asp Ser His Lys
345 35 40 45
348 Ala Gly Pro Ile Gly Ile Leu Phe Glu Leu Val His Ile Phe Leu Tyr
349 50 55 60
352 Val Val Gln Pro Arg Asp Phe Pro Glu Asp Thr Leu Arg Lys Phe Leu
353 65 70 75 80
356 Gln Lys Ala Tyr Glu Ser Lys Ile Asp Tyr Asp Lys Pro Glu Thr Val
357 85 90 95
360 Ile Leu Gly Leu Lys Ile Val Tyr Tyr Glu Ala Gly Ile Ile Leu Cys
361 100 105 110
364 Cys Val Leu Gly Leu Leu Phe Ile Ile Leu Met Pro Leu Val Gly Tyr
365 115 120 125
368 Phe Phe Cys Met Cys Arg Cys Cys Asn Lys Cys Gly Gly Glu Met His
369 130 135 140
372 Gln Arg Gln Lys Glu Asn Gly Pro Phe Leu Arg Lys Cys Phe Ala Ile
373 145 150 155 160
376 Ser Leu Leu Val Ile Cys Ile Ile Ile Ser Ile Gly Ile Phe Tyr Gly
377 165 170 175
380 Phe Val Ala Asn His Gln Val Arg Thr Arg Ile Lys Arg Ser Arg Lys
381 180 185 190
384 Leu Ala Asp Ser Asn Phe Lys Asp Leu Arg Thr Leu Leu Asn Glu Thr
385 195 200 205

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L:16 M:271 C: Current Filing Date differs, Replaced Current Filing Date

L:62 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:1,Line#:58